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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
08/956,991	10/23/1997	JULIE R. KORENBERG	P-CE-2817	9464

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EXAMINER	
SWITZER, JULIET CAROLINE	
ART UNIT	**PAPER NUMBER**
1634	

DATE MAILED: 11/19/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	08/956,991	KORENBERG, JULIE R.	
	Examiner	Art Unit	
	Juliet C. Switzer	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *31 July 2003*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,11,13-19,21-29,31-46,48 and 49* is/are pending in the application.

4a) Of the above claim(s) *11, 13-19 and 21-29* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,31-46,48 and 49* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____.
4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

RESPONSE TO APPLICANT'S AMENDMENT

1. Applicant's amendment, filed 7/31/2003, is acknowledged. Claims 33-35, 38, 41, 44, and 48 have been amended and claim 47 has been cancelled. Claims 1, 11, 13-19, 21-29, 31-46, and 48-49 are pending. Claims 11, 13-19 and 21-29 stand withdrawn from further consideration by the Examiner, 37 C.F.R. § 1.142(b) as being drawn to a nonelected invention. *Claims* 1 and 31-46, and 48-49 *are under consideration in the instant application.*

2. Applicant's amendments and arguments have been considered but are not persuasive. These are specifically addressed herein. **This action is Final.**

Claim Objections

3. The previously set forth claim objection has been overcome by cancellation of claim 47 and amendment of claim 48.

Claim Rejections - 35 USC § 112

4. The previously set forth 112 2nd paragraph rejections of claims 33, 34, 35, 36, 37, 48, and 49 have been overcome by amendment.

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 33-37 and 49are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably

convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention.

7. This rejection is reiterated from the previous office action. It has been overcome for claims 38-46 and 48 by amendment of the claims. The rejection has been modified to address newly added limitations to amended claims.

The Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement make clear that the written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the genus (Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001, see especially page 1106 3rd column).

Instant claims 33-35 (and dependent 49) are each drawn to a genus of nucleic acids which "hybridizes under high stringency conditions" to "the entire complement" various other nucleic acids recited in the claims. For claims 33 and 34, the recited nucleic acids to which the claimed nucleic acids must hybridize smaller portions of full length SEQ ID NO's disclosed in the specification. For claim 35, the recited nucleic acids to which the claimed isolated nucleic acid must hybridize is a partial cDNA sequence of the mouse homologue of the instantly disclosed molecule. The claims also set forth that the nucleotide sequence of the claimed nucleic acid

must encode a polypeptide that binds specifically an antibody, said antibody binding specifically to a molecule comprising the amino acid sequence of SEQ ID NO: 1, SEQ ID NO: 2, SEQ ID NO: 7 or SEQ ID NO: 8, as appropriate to the claim.

Although the specification discloses that the polypeptides encoded by the nucleic acids of the invention would be expected to function as neural cell adhesion molecules based upon the presence of several Ig-like C2 domains and fibronectin domains and their expression in neural crest cells (e.g., on pages 9-11, 43-44 and 56-62); this functional activity is not required of the polypeptides or polypeptide fragments encoded by the nucleic acids recited by the instant claim language.

The possible variations in the structure of the polypeptides encoded by the instantly recited nucleic acids variants is extensive. Hybridization can occur when short stretches of identity are shared between two much larger nucleic acids. In each case additional unidentified sequence may be present, and may in fact be the dominant contributor to the structure of polypeptides encoded by such nucleic acids.

There does not appear to be any requirement that relevant, identifying characteristics of the instant nucleic acids must be shared among members of the genus recited. Neither are there testable functions recited for the polypeptides encoded by these variant nucleic acids sequences to provide some correlation between a particular structure and an associated, testable, function. While the claims recite that the claimed nucleic acids must encode polypeptides that "specifically bind" recited antibodies, this recitation of "function" for the claimed polypeptide does not provide any further guidance or description of the structure of the claimed nucleic acid.

This "function" really speaks more to the structure of the claimed nucleic acid than it does to the actual function of the molecule. Applicant has not demonstrated that all of these molecules have a common functional utility, because, as discussed in this office action, this functional utility remains unclear from the evidence of record. Furthermore, it is noted that the "specific" binding to the antibody is not even defined, and may be construed a binding of an antibody to as few as three amino acids in a polypeptide. Furthermore, the binding of the antibody would be a function of the three dimensional structure of the encoded polypeptide, and thus, binding may occur even when the polypeptides are not functionally related. Thus one of skill in the art would not recognize Applicant to be in possession of the genus of nucleic acids encompassed by the instant claims.

Consequently, the claimed invention is not described in such a way as to reasonably convey to one of ordinary skill in the art that the inventor, at the time the application was filed, had possession of the invention. See Regents of the University of California v. Eli Lilly & Co., 119F3d 1559, 1569, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997). Applicant is also directed to the Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

Response to Remarks

The remarks are addressed insofar as they pertain to the claims that remain rejected. Applicant has not demonstrated possession or description of all of the nucleic acids within the claimed genus of the rejected claims. Applicant argues that the addition of the antibody binding

language provides a correlative relationship between a particular structure and a function, citing the Written Description guidelines which state that "antibody cross-reactivity" may be sufficient to show applicant was in possession of a claimed genus. However, in the instant case, applicant's recitation of "antibody cross-reactivity" of a the claimed genus is not a specific recitation, but instead a general recitation that encompasses reactivity of the encoded polypeptide with any number of possible antibodies. The "specifically binds" language used in the claims is not particularly defined in the specification, and thus, the scope of the antibodies that can be used to "test" this function is quite broad and includes any antibody that would bind the recited polypeptide as well as other polypeptides, as long as such binding is specific to the target amino acid sequence.

The genus of nucleic acids encompassed by the instant claims includes sequences which are structurally related to the disclosed sequences but which have different activity or biological function. The specification sets forth that the nucleic acids of the instant invention may encode a cell adhesion molecule or may be associated with a variety of neurological disorders. However, the claims encompass within them nucleic acids encoding molecules that are neither of these. For example, claim 33 requires that the claimed nucleic acid hybridize the nucleic acid that encodes SEQ ID NO: 11, and that "specifically" binds an antibody that also binds SEQ ID NO: 11. By requiring that the nucleic acid hybridize to the nucleic acid encoding SEQ ID NO: 11, the claim encompasses variants of SEQ ID NO: 11 for which no disclosure is provided, such as allelic variants that encode proteins that do not have the same biological or prognostic activity as SEQ ID NO: 11. The specification discloses that SEQ ID NO: 11 may be a cell adhesion molecule or may be associated with a variety of neurological disorders. The variants in the

claimed genus include molecules that share a common biological activity and thus utility with instant SEQ ID NO: 11, or that do not share such an activity and utility. Yet within this genus, applicant has only described a single set of nucleic acids, that is the set of nucleic acids that encode instant SEQ ID NO: 11. Applicant has not demonstrated possession of other nucleic acids that are alternate splice variant or allelic variants that do not share a common functionality with instant SEQ ID NO: 11. Thus, the claim and those that depend from it remain rejected for lacking adequate written description. Analogous arguments can be made for claims 34 and 35.

For these reasons and the reasons stated in the rejection, it is concluded that adequate written description does not exist for the claims as broadly drawn, and the rejection is maintained.

Claim Rejections - 35 USC § 101

8. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

9. Claims 1 and 31-46 and 48-49 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific, substantial and credible asserted utility or a well established utility.

The rejection is reiterated from the previous office action. A response to applicant's remarks follows the restatement of the rejection.

The specification discloses that the nucleic acids of SEQ ID NO:1 and SEQ ID NO:11 are transcribed in neural crest cells, that the gene responsible for these coding sequences is localized to a region of chromosome 21 associated with Down Syndrome (21q22.2-22.3), and

that the encoded polypeptide is a neural cell adhesion molecule based upon its structural homology with other neural adhesion molecules and its expression pattern (e.g., on pages 9-11, 43-44 and 56-62). The specification further teaches that SEQ ID NO: 7, SEQ ID NO: 8, and SEQ ID NO: 9 are partial cDNA clones isolated from mice using human DS-CAM cDNA clone as a probe.

The specification asserts that these nucleic acids are useful as probes for assaying for the presence and/or absence of a DS-CAM gene or as probes and primers for amplifying genes encoding DS-CAM proteins (p. 4, lines 5-10). The specification further asserts that the encoded proteins are useful for producing antibodies (p. 4 line 19). A variety of other utilities are asserted, including uses in antisense therapy and for the identification of agonisits and antagonists. These utilities are all non-specific because they are applicable to a broad class of molecules, namely proteins and nucleic acids. Any nucleic acid can be used to detect itself, and likewise, any polypeptide can be used to raise antibodies. Thus, these utilities are not sufficient to meet the standard under 101.

The specification asserts that the encoded proteins are useful in methods for regenerating damaged or severed peripheral nerves or in therapeutics (p. 4, lines 14-16 and lines 19-20). The specification teaches that members of the neural Ig-superfamily (of which the instantly disclosed molecules are postulated to be members) play critical roles in a variety of different aspects of neural development and function (p. 8, lines 17-35). The specification speculates that the DS-CAM polypeptide may be responsible for holoprosencephaly and/or several phenotypes of Down Syndrome (p. 21, lines 15-30). The specification speculates that the DS-CAM molecule can be used to diagnose a variety of diseases, including mental retardation, holoprosencephaly, agenesis

of the corpus callosum, or schizencephaly (p. 44, lines 17-30). However, the specification does not provide any evidence to support any of these utilities beyond the knowledge that this gene maps to the region of the genome that is associated with Down Syndrome and this gene is a putative cell adhesion molecule. Thus, none of these proposed utilities is considered to be a substantial utility because they are all speculative and would require further experimentation to reasonably confirm which, if any, are actual utilities of the instantly disclosed human and mouse molecules. These asserted utilities are an invitation for a researcher to further experiment to determine how to utilize the claimed nucleic acid molecules.

Claims 1 and 31-49 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

Applicant's remarks with regard to a previously set forth utility rejection are addressed herein (see papers 15 and17).

The previous rejection was for a lack of specific and did not address the issue that many of the asserted utilities, while they may be specific, are not substantial utilities because they would require further experimentation to reasonably confirm a real world utility. Applicant refers to an asserted utility of genetic testing and diagnosis of Down Syndrome on pates 43-45 of the specification. This section of the specification discusses the fact that the DS-CAM molecule is located in a region of the genome that is associated with down syndrome in both mice and humans. It goes on to suggest that in light of this fact that a number of different conditions can be diagnosed. This is considered to be an assertion of a utility that is not substantial because no

guidance or evidence is provided as to which of the list of conditions can in fact be diagnosed using the instant DS-CAM molecules. The instant utility rejection is not directed at the question of whether or not applicant has isolated an actual cDNA sequence, thus the remarks to this end are moot.

Response to Remarks

First, applicant states that the rejection herein is over a lack of credible utility, however, this is a mischaracterization of the rejection which specifically addresses the facets of specific and substantial utility. The arguments are addressed insofar as they apply. The examiner regrets the confusion caused by the use of the word "speculative" in the rejection, but maintains that the utilities set forth in the instant specification are not substantial to the claimed nucleic acids, that is, further experimentation would be required to reasonably confirm a real world use for the claimed nucleic acids.

Applicant argues that no evidence has been provided to rebut the presumption of utility, but evidence is not required, and in its absence scientific discussion and reasoning may be provided by the examiner, as was provided in the instant specification. The bottom line is that for the utilities suggested (i.e. as diagnostic or prognostic molecules) no evidence has been provided by applicant that such a utility would be applicable to the claimed invention, and it is precisely this lack of evidence that is an invitation to one of skill in the art to confirm that applicant's assertion would be tenable. This invitation to do further research to reasonably confirm the asserted utility of the claimed invention supports the argument of a lack of substantiality of the claimed invention.

Applicant's own arguments and positions on this issue underscore the concern raised by the examiner. Applicant's arguments attempt to establish that the molecules have "a role in DS and associated phenotypes," however, even if this were established in the specification, applicant has not suggested a UTILITY for the molecules, that is, what would one do with them?

Applicant cites the post filing date art of Yamakawa *et al.* to demonstrate that the data in the instant application has been presented in a peer reviewed article. First, it is noted that the reference is not prior art. Therefore these references do not support applicant's arguments that the specification was sufficient to enable the claimed invention at the time of filing since MPEP 2124 states,

> "...it is impermissible to use a later factual reference to determine whether the application is enabled or described as required under 35 U.S.C. 112, first paragraph. In re Koller, 613 F.2d 819, 823 n. 5, 204 USPQ 702, 706 n.5 (CCPA 1980). References which do not qualify as prior art because they postdate the claimed invention may be relied upon to show the level of ordinary skill in the art at or around the time the invention was made. Ex parte Erlich, 22 USPQ 1463 (Bd. Pat. App. & Inter. 1992)."

Nonetheless, it is further noted that the publication in a peer reviewed journal is not sufficient to establish a utility for the claimed invention, and in fact the article itself suggests that more work is to be done to "investigate the role of DSCAM in normal and DS development." The paper does not address the asserted utility for the claimed molecule, that is as a diagnostic of any of a number of different neurological diseases (including mental retardation, holoprosencephaly, agenesis of the corpus callosum, or schizencephaly). Further study of a molecule of interest is not a specific and substantial utility where there is no known specific and substantial utility for the disclosed molecule.

The instant situation is analogous to that which was addressed in *Brenner v. Manson*, 148 U.S.P.Q. 689 (1966), in which a novel compound which was structurally analogous to other compounds which were known to possess anti-tumor activity was alleged to be potentially useful as an anti-tumor agent in the absence of evidence supporting this utility. The court expressed the opinion that all chemical compounds are "useful" to the chemical arts when this term is given its broadest interpretation. However, the court held that this broad interpretation was not the intended definition of "useful" as it appears in 35 U.S.C. §101, which requires that an invention must have either an immediately apparent or fully disclosed "real world" utility. The court held that:

> The basic quid pro quo contemplated by the Constitution and the Congress for granting a patent monopoly is the benefit derived by the public from an invention with substantial utility. . . . [u]nless and until a process is refined and developed to this point-where specific benefit exists in currently available form-there is insufficient justification for permitting an applicant to engross what may prove to be a broad field. . . . a patent is not a hunting license. . . .[i]t is not a reward for the search, but compensation for its successful conclusion.

In this case, the conclusion of the search for a utility for the claimed molecules has not been reached.

Applicant further addresses the post-filing date art of Barlow *et al.*, which also underscores the fact that at the time of filing, there was no provided specific and substantial utility in the specification. Barlow *et al.* are further studying DSCAM molecules to determine if they are related to CNS development, suggesting that such a relationship was not previously established. Again, while this may be interesting research, it does not support a position that a specific and substantial utility for the claimed invention is provided in the instant specification.

Applicant sets forth arguments to address the examiner's concerns about the specificity of the utilities asserted in the specification. A review of the rejection will find that it was a particular set of asserted utilities, which are general to all nucleic acids, that were characterized as being non-specific utilities.

Nonetheless, it is noted that applicant states that "At the outset, it is clear that Applicant's experimentations were expressly directed to finding reagents specifically for the diagnosis and/or treatment of DS and associated phenotypes." This is not disputed, what is disputed is whether or not applicant has provided sufficient disclosure to demonstrate to one of skill in the art that this goal was achieved. Applicant's specification does not provide a diagnostic or treatment of any disease, merely provides research toward finding one. Applicant's arguments in the response are not directed toward the demonstrating that the specification teaches a particular utility, but instead are directed towards demonstrating that the DSCAM molecules are associated with downs syndrome.

The examiner does not dispute that the molecules of the instant invention map to a portion of chromosome 21 that has been shown to be associated with DS. However, this is a large portion of the chromosome (millions of base pairs) and many other genes are surely located within this region. That "interesting roles for the neural CAM in neural development and function" are suggested by the structure of DS-CAM (as stated on page 7) is not an assertion or provision of a substantial utility, but instead an invitation to further study to see if one exists. There no evidence or guidance on the record that teaches one how to use the disclosed molecules as diagnostics or therapeutics, whether or not the specification establishes that the molecules are

"related" to downs syndrome.

For these reasons, the rejection is maintained.

10. The rejections under 102 are overcome by amendment.

Conclusion

11. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

GARY BENZION, PH.D.
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600

No claims are allowed. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Juliet C. Switzer whose telephone number is 703 306 5824. The examiner can normally be reached on Monday through Friday, from 9:00 AM until 4:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, W. Gary Jones can be reached on 703 308 1152. The fax phone numbers for the organization where this application or proceeding is assigned are 703 305 3592 and (703) 305-3014.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703 308 0196.

Juliet Switzer
AU 1634

November 16, 2003